(FILE 'HOME' ENTERED AT 11:32:29 ON 01 AUG 2000)

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, SCISEARCH' ENTERED AT 11:32:33 ON 01 AUG 2000

```
L1         29500 S REV
L2          1425 S L1 AND (VECTOR OR CONSTRUCT)
L3           257 S L2 AND RRE OR (REV BINDING SUBSEQUENCE)
L4           257 S L2 AND (RRE OR (REV BINDING SUBSEQUENCE))
L5            12 S L4 AND (SPLICE AND (DONOR OR ACCEPTOR))
L6             5 DUP REM L5 (7 DUPLICATES REMOVED)
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FILE 'STNGUIDE' ENTERED AT 11:36:59 ON 01 AUG 2000

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, SCISEARCH' ENTERED AT 11:40:24 ON 01 AUG 2000

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L7            20 S REV (A) DEPENDENT (A) GENE (A) EXPRESSION
L8             6 DUP REM L7 (14 DUPLICATES REMOVED)
L9             1 S PBAR (A) EDN
L10            8 S EDN AND REV
L11            3 DUP REM L10 (5 DUPLICATES REMOVED)
L12          182 S REV AND RNASE
L13            0 S L12 AND ONCONASE
L14            0 S L12 AND SPLICE DONOR
L15           40 S L12 AND RRE
L16           19 DUP REM L15 (21 DUPLICATES REMOVED)
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US 5958768

(FILE 'HOME' ENTERED AT 11:32:29 ON 01 AUG 2000)

FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS, SCISEARCH' ENTERED AT 11:32:33 ON 01 AUG 2000

L1	29500	S	REV
L2	1425	S	L1 AND (VECTOR OR CONSTRUCT)
L3	257	S	L2 AND RRE OR (REV BINDING SUBSEQUENCE)
L4	257	S	L2 AND (RRE OR (REV BINDING SUBSEQUENCE))
L5	12	S	L4 AND (SPLICE AND (DONOR OR ACCEPTOR))

L6 ANSWER 1 OF 5 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1999292922 MEDLINE
DOCUMENT NUMBER: 99292922
TITLE: Contributions of viral **splice** sites and cis-regulatory elements to lentivirus **vector** function.
AUTHOR: Cui Y; Iwakuma T; Chang L J
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Gene Therapy Center, and University of Florida Brain Institute, College of Medicine, University of Florida, Gainesville, Florida 32610-0266, USA.
CONTRACT NUMBER: HL-59412 (NHLBI)
SOURCE: JOURNAL OF VIROLOGY, (1999 Jul) 73 (7) 6171-6.
Journal code: KCV. ISSN: 0022-538X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199909
ENTRY WEEK: 19990905
AB The mobile transgene constructs of most human immunodeficiency virus (HIV)-based lentivirus vectors currently in use contain viral long terminal repeats, a 5' untranslated region, gag sequences, and env sequences that include the **Rev**-responsive element (**RRE**). In this study, we examined the possibility of deleting HIV **splice** sites and gag and env sequences from an HIV type 1 recombinant **vector** established in our laboratory as part of our ongoing efforts to improve this **vector** system. Mutations in the major **splice donor** site (SD) markedly reduced viral RNA expression but had little effect on **vector** titer. Deletion of gag or env sequences, excluding **RRE**, led to a moderate reduction in **vector** titer. Interestingly, deletion of **RRE** slightly reduced viral RNA expression but markedly impaired **vector** function. Combined deletions of **RRE**, gag (except for the first 40 nucleotides), env, and the SD mutation resulted in a twofold increase in cytoplasmic viral RNA expression and a recovery of **vector** efficiency to approximately 50% of the wild-type level. This increase in cytoplasmic RNA levels is likely to be due, at least in part, to effects of the TE671 host cells, a human rhabdomyosarcoma cell line used for **vector** production in our system, on the cytoplasmic distribution of spliced and unspliced viral RNA. These results show that optimal lentivirus **vector** function can be maintained in the absence of multiple essential viral elements.

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:268635 CAPLUS
DOCUMENT NUMBER: 128:291139
TITLE: Construction of TRIN retroviral vectors contg. **Rev**-responsive element of HIV1 virus
INVENTOR(S): Kingsman, Susan Mary; Kingsman, Alan John
PATENT ASSIGNEE(S): Oxford Biomedica (UK) Ltd., UK; Kingsman, Susan Mary; Kingsman, Alan John
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817817	A1	19980430	WO 1997-GB2859	19971017
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9747124	A1	19980515	AU 1997-47124	19971017
GB 2331989	A1	19990609	GB 1999-4143	19971017
EP 931157	A1	19990728	EP 1997-909438	19971017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			GB 1996-21679	19961017
			WO 1997-GB2859	19971017

AB Retroviral **vector** particles having an RNA genome carrying sequences which provide in the DNA provirus at least one selected gene located within an intron in a transcription unit of the provirus, which transcription unit further comprises a polynucleotide response element which is responsive to a nucleus to cytoplasm transport factor such as HIV **Rev**. These vectors have been named TRIN (Tat and **Rev** inducible) vectors. Expression of the selected genes is thus rendered **Rev**-dependent and so is dependent upon the presence of HIV. The TRIN vectors also contain the murine leukemia virus **splice donor** site, the strong CMV promoter, a packaging signal, and the HIV U5 and R regions.

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:89371 CAPLUS
DOCUMENT NUMBER: 128:150403
TITLE: Construction of retroviral vectors for delivering viral and oncogenic inhibitors
INVENTOR(S): Raybak, Susanna M.; Cara, Andrea; Gusella, Gabriele Luca; Newton, Dianne L.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA;
Raybak, Susanna M.; Cara, Andrea; Gusella, Gabriele Luca; Newton, Dianne L.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803669	A2	19980129	WO 1997-US12637	19970717
WO 9803669	A3	19980226		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9738049	A1	19980210	AU 1997-38049	19970717
EP 917585	A2	19990526	EP 1997-935014	19970717

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.: US 1996-22052 19960722
WO 1997-US12637 19970717

AB Cell transformation vectors for inhibiting HIV and tumor growth are provided. Optionally, the vectors encode RNAses A superfamily members such as eosinophil-derived neurotoxin (EDN) and onconase. Cells transduced by the vectors and methods of transforming cells (in vitro and in vivo) using the vectors are also provided. The viral and oncogene inhibitors are typically linked to a promoter such as retroviral HIV LTR promoters, the CMV promoter, the probasin promoter, and tetracycline-responsive promoters. The method is exemplified by construction of a viral **vector** contg. a HIV **Rev** -responsive element, an encephalomycocarditis virus internal ribosome entry site, a first viral inhibitor subsequence (for immunodominant proteins such as as Tat, Gag, or **Rev**), **splice donor** site subsequence, **splice acceptor** site subsequence, the above mentioned promoter, and the EDN coding sequence. The **vector** may be packaged in a liposome and its contents transduced into CD34+ hematopoietic stem cells, CD4+ cells, and transferrin receptor+ cells. Claimed vectors include pBAR, pBAR-ONC, and pBAR-EDN.

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1994:673849 CAPLUS
DOCUMENT NUMBER: 121:273849
TITLE: Manufacture of antigens in gag protein-based particles
using a minimal retroviral expression cassette
INVENTOR(S): Czaplewski, Lloyd George
PATENT ASSIGNEE(S): British Bio-Technology Ltd., UK
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9420621	A2	19940915	WO 1994-GB281	19940211
WO 9420621	A3	19941013		

W: AU, CA, CN, DE, FI, GB, JP, KR, NO, NZ, RU, UA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

AU 9460063	A1	19940926	AU 1994-60063	19940211

PRIORITY APPLN. INFO.: GB 1993-4239 19930301
WO 1994-GB281 19940211

AB An expression cassette using a single promoter to drive expression of a gag-derived sequence from a complex retrovirus including a **rev** gene, an **RRE** element and **donor** and **acceptor** elements is described for use in the manuf. of retroviral particles presenting antigens for use in vaccines. The **construct** is arranged to ensure that the promoter is capable of driving expression of both the gag-derived sequence and the **rev**-like element. The **construct** does not contain a functional env gene. The construction of a series of such cassettes for the synthesis of tat protein is demonstrated. COS-7 cells co-transfected with one of these constructs and a CAT gene under control of a tat-responsive promoter showed high levels of expression of the CAT gene.

L6 ANSWER 5 OF 5 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 90045468 MEDLINE
DOCUMENT NUMBER: 90045468
TITLE: HTLV-1 rex and HIV-1 **rev** act through similar mechanisms to relieve suppression of unspliced RNA

expression.

AUTHOR: Itoh M; Inoue J; Toyoshima H; Akizawa T; Higashi M; Yoshida M
CORPORATE SOURCE: Department of Viral Oncology, Cancer Institute, Tokyo, Japan.

SOURCE: ONCOGENE, (1989 Nov) 4 (11) 1275-9.
Journal code: ONC. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199002

Not in

AB Human retroviruses, human T cell leukemia viruses (HTLV) and human immunodeficiency viruses (HIV), express two classes of mRNAs; fully spliced mRNA in the early phase and intron-containing mRNA in a later phase. The expressions of HTLV-1 rex and HIV **rev** by early mRNAs are essential for the later phase of expression of intron-containing gag and env mRNAs. Each two cis-acting sequences seem to be involved in these regulations: HTLV-1 rex depends on a **splice donor** (SD) and a responsible element (RXE) at the 3' end, whereas HIV **rev** depends on a specific repressive sequence (CRS) and a responsible element (**RRE**) in the intron, but does not require an SD. For analyses of these cis-acting sequences, we inserted an HIV element **RRE** into an HTLV-1 **construct** and tested the responses to HTLV-1 rex and HIV **rev** regulations. The results indicated that both rex and **rev** could regulate RNA expression of these chimeric constructs responding to an HIV **RRE**. A repressive element (CRS) was dispensable, and the intronic or exonic location of **RRE** was not important. These observations suggest that rex and **rev** could be functionally equivalent to induce cytoplasmic expression of unspliced RNA which expression is suppressed either by an SD or CRS depending on the construction.

ANSWER 3 OF 3 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 1998197329 MEDLINE
DOCUMENT NUMBER: 98197329
TITLE: Inhibition of HIV-1 replication by combined expression of gag dominant negative mutant and a human ribonuclease in a tightly controlled HIV-1 inducible vector.
AUTHOR: Cara A; Rybak S M; Newton D L; Crowley R; Rottschafer S E; Reitz M S Jr; Gusella G L
CORPORATE SOURCE: Basic Research Laboratory, NCI, NIH, Bethesda, MD, USA.
SOURCE: GENE THERAPY, (1998 Jan) 5 (1) 65-75.
Journal code: CCE. ISSN: 0969-7128.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY WEEK: 19980603

AB An HIV-1-based expression vector has been constructed that produces protective genes tightly regulated by HIV-1 Tat and **Rev** proteins. The vector contains either a single protective gene (HIV-1 gag dominant negative mutant (delta-gag)) or a combination of two different protective genes (delta-gag and eosinophil-derived neurotoxin (**EDN**), a human ribonuclease) which are expressed from a dicistronic mRNA. After stable transfection of CEM T cells and following challenge with HIV-1, viral production was completely inhibited in cells transduced with the vector producing both delta-gag and **EDN** and delayed in cells producing delta-gag alone. In addition, cotransfection of HeLa-Tat cells with an infectious HIV-1 molecular clone and either protective vector demonstrated that the HIV-1 packaging signals present in the constructs were functional and allowed the efficient assembly of the protective RNAs into HIV-1 virions, thus potentially transmitting protection to the HIV-1 target cells.